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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Stephen P. Goff and Gilda Tachedjian
Serial No.: 10/009,433 Examiner:
Filed : November 8, 2001 Group Art Unit:
For : TWO-HYBRID ASSAY THAT DETECTS HIV-1 REVERSE
TRANSCRIPTASE DIMERIZATION

1185 Avenue of the Americas
New York, New York 10036
January 23, 2002

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on PTO-1449 form attached hereto as **Exhibit A**. A copy of below listed reference 36 is attached hereto as **Exhibit 1**.

1. Baillon, J.G., et al. (1991) "A Leucine Zipper-Like Motif may Mediate HIV Reverse Transcriptase Subunit Binding", New Biol., 3:1015-1019;
2. Becerra, S., et al., (1991) "Protein-Protein Interactions of HIV-1 Reverse Transcriptase: Implication of Central and C-terminal Regions in Subunit Binding", Biochemistry, 30:11707-11719;
3. Debyser, Z. and De Clerq, E. (1996) "Chemical Crosslinking of the Subunits of HIV-1 Reverse Transcriptase", Protein Science, 5:278-286;

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4. Ding, J. et al., (1995) "Structure of HIV-1 Reverse Transcriptase in a Complex with the Non-Nucleoside Inhibitor Alpha-APA R 95845 at 2.8 A Resolution:", Structure, 3:365-379;
5. Ding, J. et al., (1995) "Structure of HIV-1 RT/TIBO R 86183 Complex Reveals Similarity in the Binding of Diverse Non Nucleoside Inhibitors", Nat. Struct. Biol., 2:407-415;
6. Divita, G., Restle, T. and Goody, R.S., (1993) "Characterization of the Dimerization process of HIV-1 Reverse Transcriptase Heterodimer Using Intrinsic Protein Fluorescence", FEBS Lett., 324:153-158;
7. Divita, G., et al., (1994) "Inhibition of Human Immunodeficiency Virus Type 1 Reverse Transcriptase Dimerization Using Synthetic Peptides Derived from the Connection Domain", J.Biol.Chem., 269:13080-13083;
8. Esnouf, R. et al. (1995) "Mechanism of Inhibition of HIV-1 Reverse Transcriptase by Non-Nucleoside Inhibitors", Nat. Struct. Biol., 2:303-308;
9. Fields, S., and Song, O. (1989) "A Novel Genetic System to Detect Protein-Protein Interaction", Nature, 340:245-246;
10. Ghosh, M. et al. (1996) "Alterations to the Primer Grip of p66 HIV-1 Reverse Transcriptase and Their Consequences for Template-primer Utilization", Biochemistry, 35:8553-8562;
11. Goel, R. et al. (1993) "Structure/Function Studies of HIV-1 (1) Reverse Transcriptase: Dimerization-Defective Mutant

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L289K", Biochemistry, 23:13012-13018;

12. Goody, R.S. (1995) "Rational Drug Design and HIV: Hopes and Limitations" Nat. Med., 1:519-520;
13. Harris, D., et al. (1998) "The p51 Subunit of Human Immunodeficiency Virus Type 1 Reverse Transcriptase is Essential in Loading the p66 Subunit on the Template Primer", Biochemistry, 37:5903-5908;
14. Hanes, S.D. and Brent, R. (1989) "DNA Specificity of the Bicoid Activator Protein is Determined by Homeodomain Recognition Helix Residue 9", Cell, 57:1275-1283;
15. Huang, H., et al. (1998) "Structure of a Covalently Trapped Catalytic Complex of HIV-1 Reverse Transcriptase: Implication for Drug Resistance", Science, 282:1669-1675;
16. Jacobo-Molina, A. et al. (1993) "Crystal Structure of Human Immunodeficiency Virus Type 1 Reverse Transcriptase Complexed With Double-Stranded DNA at 3.0 Å Resolution shows Bent DNA", J.Biol.Chem., 269:1388-1393;
17. Jacques, P.S., et al., (1994) "Modulation of HIV-1 Reverse Transcriptase Function in "Selectively Deleted" p66/p51 Heterodimers", J.Biol.Chem., 269:1388-1393;
18. Kaplana, G.V., et al., (1994) "Binding and Stimulation of HIV-1 Integrase by a Human Homolog of Yeast Transcription Factor SNF5", Science, 266:2002-2006;
19. Kaplana, G.V. and Goff, S.P., (1993) "Genetic Analysis of Homeric Interactions of Human Immunodeficiency Virus Type

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Filed : November 8, 2001
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- 1 Intergrase Using the Yeast Two-Hybrid System",
Proc.Natl.Acad.Sci.USA, 90:10593-10597;
20. Kohlsteadt, L.A., et al., (1929) "Crystal Structure of 3.5A Resolution of HIV-1 Reverse Transcriptase Complexed with an Inhibitor", Science, 256:1783-1790;
21. Legrain, P., Dokhelar, M.C. and Transy, C., (1994) "Detection of protein-protein Interactions Using Different Vectors in the Two-Hybrid System", Nucleic Acids Res., 22:3241-3242;
22. Li, X., Yuan, B., and Goff, S.P., (1997) "Genetic Analysis of Interactions Between Gag Proteins of Rous Sarcoma Virus", J.Virol., 71:5624-5630;
23. Li. X, et al., (1996) "Homomeric Interactions Between Transmembrane Proteins of Moloney Murine Leukemia Virus", J.Virol., 70:1266-1270;
24. Luban, J. et al., (1992) "Genetic Assay for Multimerization of Retroviral gag Polyproteins", J. Virol. 66:5157-5160;
25. Luban, J. et al., (1993) "Human Immunodeficiency Virus Type 1 Gag Proteins Binds to Cyclophilins A and B", Cell, 73:1067-1078;
26. Misra, H.S., Pandey, P.K., and Pandey, V.N., (1998) "An Enzymatically Active Chimeric HIV-1 Reverse Transcriptase (RT) With the Rnase-H Domain of Murine Leuemia Virus RT Exists as a Monomer", J.Biol.Chem., 273:9785-9789;
27. Morris, M.C., et al., (1999) "A New Potent HIV-1 Reverse

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Transcriptase Inhibitor A Synthetic Peptide Derived From the Interface Subunit Domains", J.Biol.Chem., 274:24941-24946;

28. Morris, M.C., et al. (1999) "The Thumb Domain of the P51-Subunit is Essential for Activation of HIV Reverse Transcriptase", Biochemistry, 28:15097-15103;
29. Ren, J., et al., (1995) "High Resolution Structures of HIV-1 RT from Four RT-Inhibitor Complexes", Nat. Struct. Biol. 2:293-302;
30. Ren, J., et al., (1995) "The Structure of HIV-1 Reverse Transcriptase Complexed with 89-chloro-TIBO: Lessons for Inhibitor Design", Structure, 3:915-926;
31. Restle, T., Muller, B., and Goody, S., (1990) "Dimerization of Human Immunodeficiency Virus Type 1 Reverse Transcriptase. A Target for Chemotherapeutic Intervention", J.Biol.Chem., 265:8986-8988;
32. Rodgers, D.W., et al. (1995) "The Structure of Unliganded Reverse Transcriptase from the Human Immunodeficiency Virus Type 1", Proc. Natl. Acad. Sci. USA, 92:1222-1226;
33. Ruden, D. M., et al. (1991) "Generating Yeast Transcriptional Activators Containing no Yeast Protein Sequences", Nature, 350:250-252;
34. Sluis-Cremer, N., et al., (2000) "Human Immunodeficiency Virus Type 1 Reverse Transcriptase Dimer Destabilization by 1-{Spiro[4"-amino-2", 2"-dioxo-1", 2"-oxathiole-5", 3'-(2', 5'-bis-o-(tert-butyl dimethylsilyl)-5-D-ribofuranosyl)]}-3-

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ethylthymine", Biochemistry, 39:1427-1433;

35. Wohrl, B.M. (1997) "Kinetic Analysis of Four HIV-1 Reverse Transcriptase Enzymes Mutated in the Primer Grip Region of p66. Implications for DNA Synthesis and Dimerization" J. Biol. Chem. , 272:17581-1757;

36. U.S. Patent No. 5,922,856,A (Fritz, et al.), July 13, 1999, (Exhibit 1).

The subject application is a National Stage Application filed under 35 U.S.C. §371 of PCT/US01/18339, filed June 6, 2001, which is a continuation-in-part of U.S. Serial No. 09/588,939, filed June 6, 2000.

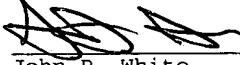
The above listed references 1-35 were submitted to and considered by the United States Patent and Trademark Office in an Information Disclosure Statement filed January 22, 2001 in connection with U.S. Serial No. 09/588,939. Accordingly, under 37 C.F.R. §1.98(d) copies of these references are not required to be provided to the United States Patent and Trademark Office, since they were previously cited by, or submitted to, the United States Patent and Trademark Office in an application relied upon for an earlier filing date under 35 U.S.C. §120. An International Search Report was issued on October 25, 2001 in connection with PCT/US01/18339. A copy of this search report is attached as Exhibit B. The above-listed references 9, 21, 28, 24, 36 were cited in the search report. A copy of reference 36 is attached hereto as Exhibit 1.


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If a telephone conference would be of assistance in advancing the prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

Pursuant to 37 C.F.R. §1.97(b)(3), no fee, is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.	
	1-23-02
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